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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Terry M. Fredeking

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BLAKELY SOKOLOFF TAYLOR & ZAFMAN
1279 OAKMEAD PARKWAY
SUNNYVALE, CA 94085-4040

EXAMINER

CHONG, YONG SOO

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

03/25/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/038,557	Applicant(s) FREDEKING ET AL.	
	Examiner YONG S. CHONG	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-16, 18-22 and 24-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-16, 18-22 and 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/15/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/5/2008 has been entered.

Claim(s) 1-12, 17, 23 have been cancelled. Claim(s) 13-16, 18-22, 24-26 are pending. Claim(s) 13 and 21 have been amended. Claim(s) 13-16, 18-22, 24-26 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of the new claim amendments. The following new rejection will now also apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-16, 18-22, 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject

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matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support for the limitation "non-diseased state" in Applicant's originally filed disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-16, 18-22, 24-26 are rejected under 35 U.S.C. 103(a) as being obvious over Jacobson et al. (*N. Engl. J. Med.* 1997 May 22, 336 (21): 1487-93) in view of Golub et al. (US Patent 6,015,804) and Applicant's admission of the prior art.

The instant claims are directed to a process comprising contacting blood or a fraction thereof in a non-diseased state with a tetracycline both *in vivo* and *in vitro* and then isolating the blood or fraction thereof.

Jacobson et al. discloses treatment of oral ulcers in HIV patients by administering thalidomide (abstract). Laboratory assays from the blood of the patients were taken to measure for cytokines and cytokine receptors. Measurements of plasma samples resulted in increased levels of tumor necrosis factor and tumor necrosis factor receptors (pg. 1488, right column, second paragraph). Jacobson et al. also teach that thalidomide is well known to inhibit production of tumor necrosis factor (pg. 1487, right column, third paragraph).

Examiner notes that taking laboratory assays from the blood of the patients inherently meets the limitation regarding isolating the blood or the fraction thereof. Furthermore, Jacobson et al. discloses measuring the plasma samples, which inherently meet the limitation regarding further processing of the isolated blood by means such as centrifugation. Upon centrifugation, blood is inherently separated into fractions containing globulin, anti-hemophilia factor, albumin, serum, and plasma.

Examiner also notes that the limitation regarding a three-fold increase of cytokine receptors as a result of administration of a tetracycline is inherent since a composition and its properties are inseparable. "Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art

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teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Furthermore, the list of diseases are considered preamble and also will not be given any patentable weight. It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish from each other. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use of a composition claim will be given no patentable weight.

It is further respectfully pointed out that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02.

Jacobson et al. teach as discussed above, however fail to specifically disclose contacting the blood with tetracycline *in vitro*.

Golub et al. teach a method of treating medical conditions characterized by excessive TNF-alpha production (abstract). Such diseases or conditions include viral infections, inflammation, diabetes, cancer, graft versus host disease, inflammatory bowel disease, arthritis, autoimmune disorders, and rheumatoid arthritis (col. 2, lines 6-18). (col. 2, lines 6-18). Golub et al. teach that such methods is useful in enhancing IL-10 production, which is known to inhibit or down regulate IL-1 and TNF-alpha production (col. 5, lines 43-45). Therefore, Golub et al. teach a method of contacting tetracycline with blood *in vitro* in order to measure increases in levels of cytokines, such as IL-10 (col. 5, lines 54-55; col. 8, lines 8-12; and examples), which then can be administered to treat the above diseases or conditions.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, for Jacobson et al. to have also performed the *in vitro* procedure of contacting the blood or a fraction thereof with a tetracycline as disclosed by Golub et al.

A person of ordinary skill in the art would have been motivated to perform the *in vitro* procedure of contacting the blood or a fraction thereof with a tetracycline or because: (1) both Jacobson and Golub et al. disclose methods of treating patients with viral infections; (2) both Jacobson and Golub et al. teach a need to inhibit production of TNF-alpha since excessive TNF-alpha production leads to various diseases; (3) Jacobson et al. teaches that thalidomide is well known to inhibit production of TNF-alpha; and (4) Golub et al. also teach the functional equivalence of tetracycline since it is also well known to inhibit production of TNF-alpha. Therefore, one of ordinary skill in

the art would have had a reasonable expectation of success in inhibiting TNF-alpha as disclosed by Jacobson et al. with tetracycline as disclosed by Golub et al. via the process of contacting the blood or a fraction thereof and subsequently isolation.

Jacobsen and Golub et al. teach as discussed above, however also fail to specifically disclose contacting non-diseased blood with tetracycline.

Applicant's admission of the prior art discusses the state of the art with regards to cytokines and its receptors in terms of various pathological conditions. Specifically, it is taught that cytokines produce a wide variety of effects on numerous cell types. Interleukin, a form of cytokine, binds to cell surface receptors, which results in a variety of effects including the production of pathological conditions resulting in chronic inflammation, septic shock, and defects in hematopoiesis. Tumor necrosis factors, (TNF) are another type of cytokines, that are primary modifiers of the inflammatory and immune reactions of animals produced in response to injury or infection. Thus, TNF play a necessary and beneficial role as mediators of host resistance to infections and tumor formation, however, overproduction or inappropriate expression of these factors can lead to a variety of pathological conditions. It is known that both types of soluble receptors can bind to TNF in vitro and inhibits its biological activity by competing with cell surface receptors for TNF binding (pg. 2-5).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, for Jacobson et al. to have

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performed the *in vivo* or *in vitro* procedure of contacting non-diseased blood or a fraction thereof with a tetracycline as disclosed by Golub et al.

A person of ordinary skill in the art would have been motivated to perform the *in vivo* or *in vitro* procedure of contacting non-diseased blood or a fraction thereof with a tetracycline as disclosed by Golub et al. because: (1) Jacobson and Golub et al. teach contacting tetracycline with blood in order to inhibit production of TNF-alpha; (2) Jacobsen et al. teach that measurements of plasma samples resulted in increased levels of TNF receptors; (3) Applicant's admission of the prior art teach that cytokine binds to cell surface receptors, which results in a variety of effects including the production of pathological conditions; and (4) that the presence of soluble receptors that bind to TNF inhibits its biological activity by competing with cell surface receptors for TNF binding. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in inhibiting or treating a pathological condition induced by overproduction of TNF by isolating a non-diseased blood or fraction thereof consisting of TNF receptors for the competitive binding of TNF with cell surface receptors. Accordingly, the skilled artisan would have carried out the procedure as taught by Jacobson and Golub et al. to isolate TNF receptors produce by tetracycline in non-diseased blood since this blood or fraction thereof is going to be used for therapeutic purposes.

Response to Arguments

Applicant argues that Jacobson et al. is directed to administration of thalidomide to HIV-infected patients. Firstly, thalidomide has been specifically excluded from the amended independent claims. Secondly, administration of thalidomide is to a diseased patient rather than a non-diseased patient.

This is not persuasive because although Jacobson et al. administers thalidomide, the secondary reference, Golub et al., was used to incorporate tetracycline. The motivation to substitute being that thalidomide and tetracycline are functional equivalent since both are well known to inhibit production of TNF-alpha.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Moreover, Applicant's arguments directed to the "non-diseased state" is moot, considering the new rejection based on Applicant's admission of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax

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phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S Chong/
Primary Examiner, Art Unit 1617

YSC